

Application No. 10/081,580  
Response to Office Notice of Non-Compliant Amendment

Customer No. 01933

Amendments to the Specification:

Please delete the heading at page 1, line 2.

Please amend the paragraph at page 3, lines 1-3 as follows:

FIG. 3 is a perspective view showing a state where a resilient ~~body~~ layer retaining member of the protein chip holding tool is released;

Please amend the paragraph at page 3, lines 8 and 9 as follows:

FIG. 6 is a view explaining another example of a supporting structure of ~~an opening and closing member~~ a slide shutter;

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Please amend the paragraph at page 3, lines 10 and 11 as follows:

FIG. 7 is a view explaining still another example of the supporting structure of the ~~opening and closing member~~ slide shutter;

Please amend the paragraph at page 3, lines 15 and 15 as follows:

FIG. 9 is a view showing a state where a substrate and a resilient ~~plate~~ layer are set on the protein chip holding tool;

Please amend the paragraph at page 3, lines 16 and 17 as follows:

FIG. 10 is a view showing a closed state of the resilient ~~body~~ layer retaining member; and

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Please amend the paragraph at page 3, lines 18 and 19 as follows:

FIG. 11 is a view showing an open state of holes in the resilient ~~body~~ layer holding member.

Please amend the heading at page 3, line 20 as follows:

~~EMBODIMENTS OF THE INVENTION~~ DETAILED DESCRIPTION

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Please amend the paragraph at page 7, line 25 to page 8,  
line 9 as follows:

The respective protein chips 33 ~~are composed of such~~  
have a structure in which a silicone rubber made resilient  
~~plate layer~~ 37 is laminated on a substrate 35 such as slide  
glass, a plastic plate, etc., made of polyethylene,  
polypropylene, etc. Holes 37a, whose number is coincident  
with the number of distribution needles 31, having the same  
matrices (8-by-12 matrices) as those of the distribution  
needles 31 are formed on the resilient ~~plate layer~~ 37, and  
the plane facing the substrate 35 is ground and flattened,  
thereby securing satisfactory contacting ability with the  
substrate 35.

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Please amend the paragraph at page 8, lines 12-22 as follows:

A base plate 39 ~~that constitutes a substrate holding member of the protein chip holding tool 7~~ is sized so that holds five substrates 35 whose ~~lengthwise direction is oriented in the left and right direction in the drawing, for example, can be disposed in the lengthwise orthogonal direction (forward and backward direction), wherein on as~~ shown in FIG. 9. On the upper plane thereof of the base plate 39, downward facing recesses 41 which are shaped so as to be coincident with the respective substrates 35 are provided with adequate spacing in the ~~forward and backward~~ lengthwise direction of the base plate 39, and the substrates 35 are held in the respective downward facing recesses 41.

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Please amend the paragraph at page 8, line 23 to page 9,  
line 2 as follows:

Notched parts 43 are formed in the base plate 39 such  
~~that is positioned in the respective downward facing~~  
~~recesses 41, whereby a finger, etc. for example, is~~ may be  
inserted into the respective notched parts 43, thereby  
enabling removal of the substrates 35 held in the downward  
facing recesses 41.

Please amend the paragraph at page 9, lines 3-8 as follows:

A ~~holding plate lid~~ 45 that constitutes a resilient  
~~body layer~~ holding member is supported at the left side end  
part ~~, shown in the drawing,~~ of the base plate 39 as shown  
in Figs. 3 and 9 so that the ~~holding plate lid~~ 45 moves and  
turns between the position covering the upper surface of the  
base plate 39 and the position separated therefrom.

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Please amend the paragraph at page 9, lines 9-15 as follows:

Upward facing recesses 51 that are sized to be coincident with the downward facing recesses 41 are formed on the bottom (the plane ~~corresponding to~~ facing the base plate 39) of the ~~holding plate~~ lid 45 so that these recesses 51 are faced to the respective downward facing recesses 41. And the resilient ~~plate layers~~ 37 that ~~constitutes a part~~ constitute parts of the protein ~~chip chips~~ 33 ~~is~~ are held on in the upward facing recesses 51.

Please amend the paragraph at page 9, lines 16-20 as follows:

A number of holes 45a that function as openings are provided ~~on in~~ the ~~holding plate~~ lid 45, in areas corresponding to the upward facing recesses 51, so as to be coincident with the respective holes 37a ~~at in~~ the resilient ~~plates~~ layers 37 that are retained in the respective upward facing recesses 51.

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Please amend the paragraph at page 9, line 21 to page 10,  
line 12 as follows:

~~An opening and closing plate~~ A slide shutter 53 is supported on the upper surface of the ~~holding plate lid~~ 45 so as to be movable in the left and right direction shown in the ~~drawing (FIG. 4)~~ FIG. 4 over ~~approx.~~ approximately half of the width distance between the holes 45a in the left and right direction of the ~~respective holes 45a at the holding plate 45~~ FIG. 4. A number of slits 53a are formed ~~on in~~ the ~~corresponding opening and closing plate~~ slide shutter 53 so as to become coincident with the respective holes 45a when the slits 53a are moved to the left side, as shown in the ~~drawing (FIG. 4)~~ FIG. 4, on the ~~holding plate lid~~ 45. The ~~opening and closing plate~~ slide shutter 53 locates the respective slits 53a between the respective holes 45a and ~~closes to close the same holes~~ when the ~~opening and closing plate~~ slide shutter 53 is moved to the right side, ~~shown in the drawing (FIG. 4)~~, with respect to the ~~holding plate lid~~ 45. ~~while the opening and closing plate~~ The slide shutter 53 exposes the respective holes 37a of the resilient plate layers 37 to the outside via the slits 53a and ~~hole~~ respective holes 45a when the slits 53a are positioned over the holes 45a.



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Please amend the paragraph at page 10, line 13 to page 11,  
line 7 as follows:

The structure for supporting ~~a slide of the opening and closing plate~~ slide shutter 53 with respect to the holding plate lid 45 may be ~~any one of a structure for movably slidably~~ supporting the end part of the ~~opening and closing plate~~ slide shutter 53 on a supporting plate 54 secured at both ends of the ~~holding plate~~ lid 45 in the lengthwise direction thereof as shown in FIG. 1. Alternatively, a ~~structure in which~~ the respective end portions of the ~~opening and closing plate~~ slide shutter 53 in the lengthwise direction ~~are~~ may be folded to be like an inverted C shape with regard to the cross section thereof and the end portions ~~are caused to~~ may be movably slidably engaged with the respective end portions of the ~~holding plate~~ lid 45 and support the same as shown in FIG. 6. Alternatively, and a ~~structure in which~~ slits 53b having a length coincident with the moving ~~width~~ amount of the ~~opening and closing plate~~ slide shutter 53 ~~are~~ may be formed on the respective end portions of the ~~opening and closing plate~~ slide shutter 53

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in the lengthwise direction as shown in FIG. 7, and engaging members 53c such as stepped axes and stepped screws, etc., ~~which are~~ may be inserted into the respective slits 53b, ~~are~~ provided and movably so that the slide shutter 53 is slidably supported at the ~~holding plate~~ lid 45.

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Please amend the paragraph at page 11, lines 8-19 as follows:

An operating arm 55 having an engaging ~~portion~~ hole 55a is formed so as to protrude outward at the respective forward and backward end portions at the right side, as shown in ~~the drawing (FIG. 9)~~ FIG. 9, of the ~~opening and closing plate slide shutter~~ 53. An ~~engaging portion 57a of~~ an operating member 57, such as an electromagnetic solenoid and a pneumatic cylinder, ~~which~~ is attached to the respective forward and backward end portions, as shown in ~~the drawing (FIG. 9)~~ FIG. 9, of the base plate 39. An engaging portion 57a of each operation member 57 is engaged with the respective engaging holes hole 55a, wherein such that the opening and closing plate slide shutter 53 is opened and closed with respect to the ~~holding plate lid~~ 45 by actuation of the corresponding operating member 57.

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Please amend the paragraph at page 11, line 20 to page 12,  
line 12 as follows:

A locking member 59 at the right side, as shown in the ~~drawing (FIG. 10)~~ FIG. 10, of the base plate 39 is supported so as to be turnable. The ~~corresponding~~ locking member 59 is composed of a locking arm portion 59a, which is brought into contact with the entirety of the right end portion of the lid 45, ~~shown in the drawing (FIG. 9)~~, in the forward and backward lengthwise direction of the ~~holding plate lid 45~~, when the lid 45 turned to the position covering the upper surface of the base plate 39 and ~~[[a]]~~ an axial supporting arm portion 59b, which ~~suspends~~ extends from both the end parts of the ~~corresponding~~ locking arm portion 59a ~~in the forward and backward direction~~ and is axially supported on the base plate 39. When the locking arm portion 59a is brought into contact with the upper surface at the right side end, ~~shown in the drawings~~, of the ~~holding plate lid 45~~ and locked thereat, the axial supporting member 59 causes the respective resilient plates layers 37, which are held on the ~~holding plate lid 45~~, to be adhered to the respective substrates ~~45~~ 35, which are retained on the base plate 39.

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Please amend the paragraph at page 12, lines 13-25 as follows:

Where the length of the axial supporting arm portion 59b is made short to cause the locking member 59 to be tightly adhered to the ~~holding plate~~ lid 45, maneuverability is worsened when locking and unlocking the locking arm portion 59a. To prevent the above from occurring, as shown in FIG. 8, a pressing member 61 ~~(FIG. 6 shows a case where a plate spring is used as a pressing member)~~ such as a plate spring or a pin having a spring, etc., is provided at the locking arm portion 59a, and the ~~holding plate~~ lid 45 is pressed in the closing direction by a resilient force of the corresponding pressing member 61, wherein the adhesivity between the substrate 35 and the resilient ~~plate~~ layer 37 may be increased.

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Please amend the paragraph at page 13, line 24 to page 14,  
line 7 as follows:

On the other hand, in a state where the ~~holding plate~~  
lid 45 is moved and turned to an open position with respect  
to the base plate 39 as shown in FIG. 9, substrates 35 are  
set in respective downward facing recesses 41 of the base  
plate 39 and resilient ~~plates~~ layers 37 are set in  
respective upward facing recesses 51 of the ~~holding plate~~  
lid 45. After that, the ~~holding plate~~ lid 45 is turned and  
moved to the base plate 39 side as shown in FIG. 1, and the  
locking member 59 is locked at the tip end portion of the  
~~holding plate~~ lid 45.

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Please amend the paragraph at page 14, lines 8-18 as follows:

At this time, the resilient ~~plates~~ layers 37 are resiliently deformed by locking of the locking member 59 and ~~the locking member 59 is~~ are brought into close contact with the ~~substrate~~ substrates 35. Further, the engaging portions 57a of the operating ~~member~~ members 57 ~~is~~ are engaged in the engaging holes 55a in the above-described closed state. Also, as shown in FIG. 10, the ~~opening and closing plate~~ slide shutter 53 is moved in the left and right directions, ~~shown in the drawing,~~ slid on the upper surface of the ~~holding plate~~ lid 45, wherein ~~such that~~ the respective slits 53a ~~is~~ are located between the holes 45a, and the respective holes 37a are closed.

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Please amend the paragraph at page 14, lines 19-24 as follows:

The ~~opening and closing plate~~ slide shutter 53 is moved slid in the leftward direction shown in, for example, FIG. 11, by actuating the operating member 57 in the above-described state, and the respective slits 53a are made coincident with the respective holes 45a of the ~~holding~~ plate lid 45, ~~wherein such that~~ the respective holes 37a of the resilient plate layers 37 are exposed to the outside.



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Please amend the paragraph at page 14, line 25 to page 15,  
line 12 as follows:

After, in the above-described state, the respective distribution needles 31 are caused to face the respective exposed holes 37a of the resilient ~~plates~~ layers 37 secured in the first row in the forward and backward direction via the slits 53a and holes 45a by controlling and moving the moving body 29, the moving body 29 is lowered, and the tip end parts of the respective distribution needles 31 are caused to advance into the respective holes 37a. Thereafter, the pistons in the respective syringes 25a are slightly moved in the micron level, whereby the protein test sample solution accumulated in the syringes 25a is discharged to the respective distribution needle 31 side and is dispersed into the respective holes 37a.

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Please amend the paragraph at page 15, lines 13-22 as follows:

At this time, the amount of movement of the pistons in the syringes 25a is controlled so that the amount of protein test sample solution accumulated in the holes 37a becomes 0.5 through 10  $\mu$ l, preferably 5  $\mu$ l. Also, since the resilient ~~plate~~ layers 37 ~~is~~ are brought into close contact with the upper ~~surface~~ surfaces of the ~~substrate~~ substrates 35 at a high degree of airtightness as described above, the protein test sample solution accumulated in the holes 37a is prevented from leaking, whereby respective protein test sample solutions accumulated in the respective holes 37a are prevented from contaminating each other.

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Please amend the paragraph at page 15, line 23 to page 16,  
line 9 as follows:

Next, the moving body 29 is moved in the forward and backward direction after the respective distribution needles 31 are removed from the holes 37a of the resilient plate layer 37 at the first row in the forward and backward direction by vertically moving the moving body 29, and the moving body 29 is caused to face the respective holes 37a of the resilient ~~plate~~ layer 37 at the second row in the forward and backward direction. After that, an appointed amount of protein test sample solution is distributed into the respective holes 37a of the resilient ~~plate~~ layer 37 at the second row in the forward and backward direction by actions similar to those described above.

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Please amend the paragraph at page 16, lines 10-19 as follows:

By repeating the above-described actions, an appointed amount of a protein test sample solution is distributed into the holes 37a of the respective resilient ~~plates~~ layers 37 closely adhered to the respective substrates 35, and five protein chips 33 are produced. After that, the ~~opening and closing plate~~ slide shutter 53 is moved in the rightward direction, ~~shown in the drawing (FIG. 9)~~ FIG. 9 by moving the operating member 57 back, wherein the respective slits 53a are located between the respective ~~slits~~ holes 45a, and the respective holes 37a are closed.

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Please amend the paragraph at page 16, line 20 to page 17,  
line 1 as follows:

Thereby, it is possible to prevent the protein of the protein test sample solutions accumulated in the respective holes 37a of the resilient ~~plates~~ layers 37 in the protein chips 33 from being denatured due to drying in a short time and being inactivated, whereby it is possible to produce protein chips 33 by which a reaction of a preparation to be tested in a liquid phase can be securely carried out.

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Please amend the paragraph at page 19, line 16 to page 20,  
line 2 as follows:

After the above-described sucking operation is completed, the changer board 21 of the suction and discharge changer device 17 is moved and the flow line is changed so that the respective syringes 25a of the suction and discharge device 25 are able to communicate with the respective distribution needles 31. After that, the moving body 29 is controlled and moved, whereby the respective distribution needles 31 are respectively faced to the respective holes 37a of the resilient ~~plate~~ layers 37 at the protein chips 33 that are held by the protein chip holding tool 7, for example, at the first row in the forward and backward direction.

Please amend the paragraph at page 20, lines 3-6 as follows:

At this time, the ~~opening and closing plate~~ slide shutter 53 is moved by operating the operating member 57 to cause the holes 37a of the resilient ~~plate~~ layers 37 of the respectively produced protein chips 33 to be exposed to the outside.

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Please amend the paragraph at page 20, line 15 to page 21,  
line 1 as follows:

After, by repeating the above-described action, the preparation solution to be tested is discharged, at an appointed ratio of amount, into the holes 37a of the resilient ~~plate~~ layers 37 at the respective protein chips 33 that are set on the protein chip holding tool 7, the operating member 57 is moved back in order to ~~move~~ slide the ~~opening and closing plate~~ slide shutter 53 into the closing direction, wherein the respective holes 37a of the resilient ~~plate~~ layers 37 are closed, and the protein test samples, which are in the holes 37a of the respective resilient ~~plates~~ layers 37, and a preparation solution to be tested, are reacted in the liquid phase in the above-described state.

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Please amend the paragraph at page 21, lines 2-8 as follows:

In the above-described reaction, since the respective holes 37a of the resilient ~~plates~~ layers 37 are interrupted by the atmosphere by the ~~opening and closing plate slide shutter~~ 53, the protein test sample solutions, which are accumulated in the respective holes 37a, and the preparation solutions are prevented from being dried, wherein it is possible to securely carry out a liquid phase reaction.



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Please amend the paragraph at page 21, lines 11-21 as follows:

1. By operating to close the ~~holding-plate~~ lid 45, in which the resilient ~~plate~~ layers 37 ~~is~~ are set, with respect to the base plate 39 on which the ~~substrate~~ substrates 35 ~~is~~ are set, it is possible to bring ~~both of these~~ the resilient layers 37 and the substrates 35 into close contact with each other. At this time, the adhesivity of both can be increased by resiliently deforming the resilient ~~plate~~ layers 37 with respect to the ~~substrate~~ substrates 35, wherein it is possible to prevent the protein test sample solutions distributed in respective holes 37a of the resilient ~~plate~~ layers 37 and a preparation solution to be tested from leaking, and it is possible to prevent both of the solutions from contaminating each other.

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Please amend the paragraph at page 21, line 22 to page 22,  
line 3 as follows:

2. Since the matching planes of the resilient ~~plate~~ layers  
37 and the ~~substrate~~ substrates 35 are polished and  
flattened at a high degree of accuracy, the adhesivity of  
both can be increased, and it is possible to prevent the  
protein test sample solutions distributed in respective  
holes 37a and a preparation solution to be tested from  
leaking, and it is possible to prevent both of the solutions  
from contaminating each other.

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Please amend the paragraph at page 22, lines 4-18 as follows:

3. By moving sliding the opening and closing plate slide shutter 53 to expose the respective holes 37a of the resilient plate layers 37 when producing protein chips and analyzing a preparation to be tested by the produced protein chips, it becomes possible to distribute the protein test sample solutions and preparation solution to be tested, and it is possible to prevent the protein test samples and preparation solution to be tested [[,]] from being denatured or inactivated due to drying of the distributed protein test samples and the preparation solution, which is added thereto, by closing the holes 37a of the resilient plate layers 37 by causing the opening and closing plate sliding shutter 53 to move slide after the protein chips are produced or when executing a reaction. That is, analysis of the preparation solutions to be tested can be effectively carried out.

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Please amend the paragraph at page 22, line 19 to page 23,  
line 2 as follows:

4. Since the ~~holding plate~~ lid 45 is pressed to the base plate 39 side by the pressing member 61 of the locking member 59 and the resilient ~~plate~~ layers 37 ~~is~~ are brought into close contact with the ~~substrate~~ substrates 35 at a high degree of airtightness, it is possible to prevent protein test sample solutions, which are distributed into the respective holes 37a, and a preparation solution to be tested from leaking, and it is also possible to prevent the solutions from contaminating each other.

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Please amend the paragraph at page 23, lines 5-11 as follows:

1. Although, in the above description, ~~such a structure may be employed,~~ is described in which five substrates 35 are set on a single base plate 39, a plurality of lines of substrates 35, each line consisting of five substrates, may be set. In this case, ~~such a structure is employed, in which a holding plate 45 having an opening and closing plate 35 a~~ lid may be provided with slide shutter secured per line, and a locking member 59 ~~are provided.~~

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Please amend the paragraph at page 23, lines 12-20 as follows:

2. Although, in the above description, ~~such~~ a structure is employed, described in which a number of holes 45a coincident with the number of holes 37a of the held resilient plate layers 37 are provided ~~on~~ in the holding plate lid 45, a plurality of slits ~~45b composed of having~~ a length coincident with the entirety of a plurality of holes 37a in the row direction of ~~the~~ a resilient layer 37 may be employed. Also, slits 53a of the ~~opening and closing plate slide shutter~~ slide shutter 53 may be made into ~~at least~~ holes coincident with the number of holes 37a of the resilient plate layers 37.

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Please amend the paragraph at page 23, line 21 to page 24,  
line 1 as follows:

3. Although, in the above description, the ~~opening and closing plate slide shutter 53~~ is selectively moved ~~slid~~ by the operating member 57 and the holes 37a of the resilient plate layers 37 are opened and closed, the operating member 57 is not necessarily requisite in the composition of the present invention. Instead, an operator may manually ~~move slide~~ the ~~opening and closing plate slide shutter 53~~.

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Please amend the paragraph at page 24, lines 2-12 as follows:

4. Although, in the above description, ~~such a structure is employed, described~~ in which the ~~opening and closing plate slide shutter~~ 53 is opened and closed by normal and reverse operations of the operating member 57, another structure may be employed, in which a tension spring or a compression spring is ~~employed provided~~ at the ~~holding plate lid~~ 45 and the ~~opening and closing plate slide shutter~~ 53. In this case, the opening and closing plate slide shutter 53 is moved slid in the opening direction by the operating member to open the holes 37a while the ~~opening and closing plate slide shutter~~ 53 is always moved urged to slide in the closing direction by a resilient force of these spring members with respect to the ~~holding plate lid~~ 45.